REMARKS

Claims

Applicants note that claims up to claim 23 were examined. Applicants on June 1, 2005, filed a supplemental reply where claims 24 and 25 were added. For the Examiner's convenience a copy of said supplemental reply is attached.

The Rejections Under 35 USC § 112

Claim 16 is cancelled without prejudice or disclaimer and claim 13 is amended.

In claim 20, the term "obtainable" is replaced with "obtained." Nevertheless, the term obtainable does not render a claim indefinite. It is clear to one or ordinary skill in the art that what follows is positively claimed. The term merely reflects that the product of a process is claimed, which claim leaves open the possibility that the same product may be obtained by other methods.

The Rejections Under 35 USC § 103

In the Office Action it is stated that this rejection is over Grabowski, but the discussion that follows is over Zettler. Applicants believe that the reference to Grabowski is in error and that the rejection is over Zettler.

Zettler provides general background information for melt extrusion. It teaches a very large number of possible active ingredients (see column 5, lines 42 to column 6, lines 47) and a very large number of possible additional classes of ingredients, within each of which are a lager number of specifically named possible compounds (see column 3, line 45 to column 5, lines 17). Among the very large number of possible active ingredients, estradiol and ethinylestradiol are mentioned. Preferred active ingredients in the reference do not include estradiol or ethinylestradiol. See column 6, lines 48-51 and the examples. Zettler teaches a very large number of possible suitable binders, among which is polyvinylpyrrolidone. The Office Action points to column 4, lines 44-47 and alleges that triglycerides are specified. However, These triglycerides are not polyalcohols esterified with a fatty acid. Zettler teaches on column 4, lines 13-14 that the mixture preferably contains no plasticizer. Taken as a whole, there isn't adequate

teaching or suggestion in this reference to motivate one of ordinary skill in the art to prepare the claimed invention herein.

Zettler provides a vast number of possible active ingredients among which no teaching or suggestion is provided for estradiol or ethinylestradiol, but only a pointing away by providing preferences and examples to other actives. Zettler also explicitly points away from using plasticizers as a whole and fails to mention polyalcohols esterified with a fatty acid. Without any guidance toward the present invention to one of ordinary skill in the art among the vast number of possibilities within this reference, there is no obviousness.

The Rejections Under 35 USC § 102

Meignant is alleged to anticipate. The Office Action points to the formulation disclosed on column 6, lines 15-20. In this formulation among the ingredients, solid triglycerides are pointed out. However, these solid triglycerides are not polyalcohols esterified with a fatty acid. Accordingly there is no anticipation. Additionally, there is also no obviousness as nothing in this reference teaches or even suggests polyalcohols esterified with a fatty acid as possible ingredients in formulations.

Applicants do not believe any fees are due for filing this paper. However, if the Examiner concludes otherwise, the Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Date: **November 29, 2005**

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

HULSMANN et al.

Examiner: WEBMAN, Edward J.

Serial No.: 09/937,302

Group Art Unit: 1617

Filed: 3/27/2002

Title: **PHARMACEUTICAL COMPOSITION CONTAINING AN EXTRUSION ADDITIVE**

SUPPLEMENTAL AMENDMENT

Mail Stop AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In addition to the Reply filed 22 November 2004, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 8 of this paper.

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. **(Previously Presented)** A pharmaceutical composition obtainable by mixing at least one active ingredient comprising a 17-β-estradiol or ethinylestradiol with at least one extrusion additive from a polyalcohol esterified with a fatty acid wherein the extrusion additive comprises a sugar fatty acid ester, a polyethylene glycol fatty acid ester or a glycerol fatty acid ester, and an adjuvant comprising polyvinylpyrrolidone, polyethylene glycol, vinylpyrrolidonevinyl acetate copolymer or a mixture thereof and joint melt extruding.

2. **(Canceled)**

3. **(Canceled)**

4. **(Previously Presented)** A pharmaceutical composition according to claim 1, wherein the fatty acid has 1 to 31 carbon atoms and are unbranched and/or branched and/or saturated and/or unsaturated.

5. **(Canceled)**

6. **(Previously Presented)** A pharmaceutical composition according to claim 1, wherein the melt extrusion is carried out without additional heat input.

7. **(Previously Presented)** A pharmaceutical composition according to claim 1 wherein the extrusion additive is saccharose monopalmitate and the composition is obtainable by mixing 17-β-estradiol, polyvinylpyrrolidone and saccharose monopalmitate and joint melt extruding at 60°C.

8. **(Previously Presented)** A pharmaceutical composition according to claim 1 wherein the extrusion additive is glycerol tribehenate and the composition is obtainable by mixing 17-β-estradiol, polyvinylpyrrolidone and glycerol tribehenate and joint melt extruding at 60°C.

9. **(Previously Presented)** A pharmaceutical composition according to claim 1 wherein the extrusion additive is saccharose monopalmitate and the composition is obtainable by mixing ethinylestradiol, polyvinyl-pyrrolidone and saccharose monopalmitate and joint melt extruding at 60°C.

10. **(Previously Presented)** A process for the production of a pharmaceutical composition comprising joint melt extruding a mixture comprising at least one active ingredient of 17-β-estradiol or ethinylestradiol with at least one extrusion additive of a polyalcohol esterified with a fatty acid.

11. **(Previously Presented)** A process according to claim 10, wherein the melt extrusion is carried out without heat input.

12. **(Previously Presented)** A process according to claim 10, further comprising grinding the extruded mixture and processing into a pharmaceutical agent with a pharmaceutically compatible adjuvant or additive.

13. **(Previously Presented)** A pharmaceutical agent comprising a pharmaceutical composition according to claim 1 and a pharmaceutically compatible adjuvant or additive.

14. **(Canceled)**

15. **(Previously Presented)** A process according to claim 11, further comprising grinding the extruded mixture and processing into a pharmaceutical agent with a pharmaceutically compatible adjuvant or additive.

16. **(Previously Presented)** A pharmaceutical composition according to claim 1, wherein the composition comprises a low-dose amount of the at least one active ingredient.

17. **(Previously Presented)** A pharmaceutical composition according to claim 1, wherein the composition comprises 0.025% of at least one active ingredient relative to a single dose.

18. **(Previously Presented)** A pharmaceutical composition according to claim 1, wherein the extrusion additive is from polyalcohols esterified with fatty acids.

19. (Previously Presented) A pharmaceutical composition according to claim 1, wherein the extrusion additive consists of a sugar fatty acid ester, a polyethylene glycol fatty acid ester or a glycerol fatty acid ester, the at least one active ingredient consists of 17-β-estradiol or ethinylestradiol, and the adjuvant consists of polyvinylpyrrolidone, polyethylene glycol, vinylpyrrolidonevinyl acetate copolymer, or a mixture thereof.

20. (Previously Presented) A pharmaceutical composition obtainable by extruding a mixture comprising 17-β-estradiol or ethinylestradiol and a sugar fatty acid ester, a polyethylene glycol fatty acid ester or a glycerol fatty acid ester.

21. (Previously Presented) A process according to claim 10, wherein the extrusion additive is from polyalcohols esterified with fatty acids.

22. (Previously Presented) A pharmaceutical composition according to claim 1, wherein the pharmaceutical composition is a solid dispersion.

23. (Previously Presented) A mixture comprising 17-β-estradiol or ethinylestradiol and a sugar fatty acid ester, a polyethylene glycol fatty acid ester or a glycerol fatty acid ester.

Please add the following new claims:

--24. (New) A pharmaceutical composition according to claim 1, further comprising an active ingredient of:

acebutolol, acetylcysteine, acetylsalicylic acid, aciclovir, alprazolam, albumin, alfacalcidol, allantoin, allopurinol, ambroxol, amikacin, amiloride, aminoacetic acid, amiodarone, amitriptyline, amlodipine, amoxicillin, ampicillin, ascorbic acid, aspartame, astemizole, atenolol, beclometasone, benserazide, benzalkonium hydroxide, benzocaine, benzoic acid, betamethasone, bezafibrate, biotin, biperiden, bisoprolol, bromazepam, bromhexine, bromocriptine, budesonide, bufexamac, buflomedil, buspirone, caffeine, camphor, captopril, carbamazepine, carbidopa, carboplatin, cefaclor, cefalexin, cefadroxil, cefazolin, cefixime, cefotaxime, ceftazidine, ceftriaxone, cefuroxime axetil, chloramphenicol, chlorhexidine, chloropheniramine, chlorthalidone, choline, ciclosporin, cilastatin, cimetidine, ciprofloxacin, cisapride, cisplatin, clarithromycin, clavulanic acid, clomipramine, clonazepam, clonidine, clotrimazole, clozapine, codeine, colestyramine, cromoglycic acid, cyanocobalamin, cyproterone, desogestrel, dexamethasone, dexpanthenol, dextromethorphan, dextropropoxyphene, diazepam, diclofenac, digoxin, dihydrocodeine, dihydroergotamine, diltiazem, diphenhydramine, dipyridamole, dipyrone, disopyramide, domperidone, dopamine, enalapril, ephedrine, epinephrine, ergocalciferol, ergotamine, erythromycin, etoposide, eucalyptus globulus, famotidine, felodipine, fenofibrate, fenoterol, fentanyl, flavin mononucleotide, fluconazole, flunarizine, fluorouracil, fluoxetine, flurbiprofen, furosemide, gemfibrozil, gentamicin, ginkgo biloba, glibenclamide, glipizide, glycyrrhiza glabra, guaifenesin, haloperidol, heparin, hyaluronic acid, a hydrochlorothiazide, hydrocodone, hydrocortisone, hydromorphone, ipratropium hydroxide, ibuprofen, imipenem, indomethacin, iohexol, iopamidole, isosorbide dinitrate, isosorbide mononitrate, isotretinoin, ketotifen, ketoconazole, ketoprofen, ketorolac, labetalol, lactulose, lecithin, levocarnitine, levodopa, levoglutamide, levonorgestrel, levothyroxine,

lidocaine, lipase, lisinopril, loperamide, lorazepam, lovastatin, medroxyprogesterone, menthol, methotrexate, methyldopa, methylprednisolone, metoclopramide, metoprolol, miconazole, midazolam, minocycline, minoxidil, misoprostol, morphine, a multivitamin, a mineral, nystatin, N-methylephedrine, naftidrofuryl, naproxen, neomycin, nicardipine, a nicergoline, nicotinamide, nicotine, nicotinic acid, nifedipine, nimodipine, nitrendipine, nizatidine, norethisterone, norfloxacin, norgestrel, nortriptyline, ofloxacin, omeprazole, ondansetron, pancreatin, panthenol, pantothenic acid, paracetamol, penicillin G, penicillin V, phenobarbital, a pentoxifylline, phenylephrine, phenylpropanolamine, phenytoin, piroxicam, polymyxin B, povidone-iodine, pravastatin, prazosin, prednisolone, propafenone, propranolol, pseudoephedrine, pyridoxine, quinidine, ramipril, ranitidine, reserpine, retinol, riboflavin, rifampicin, rutoside, saccharin, salbutamol, salcatonin, salicylic acid, selegiline, simvastatin, somatropin, sotalol, spironolactone, sucralfate, sulbactam, sulfamethoxazole, sulpiride, tamoxifen, tegafur, teprenone, terazosin, terbutaline, terfenadine, theophylline, thiamin, ticlopidine, timolol, tranexamic acid, tretinoin, triamcinolone acetonide, triamterene, trimethoprim, troxerutin, uracil, valproic acid, vancomycin, verapamil, vitamin E, volic acid, or zidovudine.

25. (New) A pharmaceutical composition comprising at least one active ingredient comprising a 17-β-estradiol or ethinylestradiol, at least one extrusion additive from a polyalcohol esterified with a fatty acid wherein the extrusion additive comprises a sugar fatty acid ester, a polyethylene glycol fatty acid ester or a glycerol fatty acid ester, and an adjuvant comprising polyvinylpyrrolidone, polyethylene glycol, vinylpyrrolidonevinyl acetate copolymer or a mixture thereof.--

REMARKS

The principle purpose of this amendment is to add claims and clarify that the claimed pharmaceutical composition can optionally include other components, such as one or more active ingredients besides 17-β-estradiol, ethinylestradiol, or a mixture thereof. Hence, these amendments do not narrow the scope of the claims.

Applicants do not believe any fees are due for filing this paper. However, if the Examiner concludes otherwise, the Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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